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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/992,538	11/19/2001	Kuniaki Nagayama	116-011843	4427
26161	7590	11/16/2004	EXAMINER	
FISH & RICHARDSON PC 225 FRANKLIN ST BOSTON, MA 02110			SISSON, BRADLEY L	
			ART UNIT	PAPER NUMBER

1634

DATE MAILED: 11/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/992,538

Applicant(s)

NAGAYAMA, KUNIAKI

Examiner

Bradley L. Sisson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 October 2004.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-34 is/are pending in the application.
- 4a) Of the above claim(s) 32-34 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-31 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Election/Restrictions

1. Claims 32-34 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 27 October 2004.
2. Applicant's election without traverse of Group I, claims 1-31, in the reply filed on 27 October 2004 is acknowledged.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Attention is directed to the decision in *University of Rochester v. G.D. Searle & Co.* 68 USPQ2D 1424 (Fed. Cir. 2004) at 1428:

To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. *Vas-Cath*, 935 F.3d at 1563; see also *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572 [41 USPQ2d 1961] (Fed. Cir. 1997) (patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude

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that "the inventor invented the claimed invention"); In re Gosteli, 872 F.2d 1008, 1012 [10 USPQ2d 1614] (Fed. Cir. 1989) ("the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed"). Thus, an applicant complies with the written-description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572.

5. For convenience, claims 1 and 2, the only independent claims under consideration, are reproduced below.

1. A method of determining the sequence of bases of a DNA or RNA, comprising the steps of:

producing a magnified image of an elongated single-chain DNA or RNA by a transmission electron microscope; and

discriminating base-specific labels of heavy elements using said magnified image.

2. A method of determining the sequence of bases of a DNA or RNA, comprising the steps of:

(a) forming a support film, on which an elongated single-chain DNA or RNA is held, on an electron microscope grid;

(b) treating bases of the elongated single-chain DNA or RNA on the support film formed on said microscope grid with base derivatives each containing a heavy element or elements to form base pairs, thus forming base-specific labels of heavy elements; and

(c) observing the elongated single-chain DNA or RNA through a transmission electron microscope and discriminating said base-specific labels of heavy elements using an obtained magnified image.

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6. As presently worded, claims 1, 2, and claims 3-31 that depend therefrom, have been interpreted as encompassing the determination of any and all nucleic acids, without regard to their length, purity, or the presence of any amount of concentration of contaminants.

7. A review of the specification fails to find an adequate written description of where any length of any nucleic acid has been accurately and reproducibly sequenced by the claimed method. While the method calls for the use of labels along with a transmission electron microcopy, the claimed method does not require that unbound label be removed prior to discriminating, or that the nucleic acid actually be labeled when the label is present. The specification does not provide an adequate written description as to how the requisite discrimination can be performed when no label is present. Assuming *arguendo* that the claims were to be drawn to a method of sequencing where the label was bound to each nucleotide, and unincorporated label were removed, the specification does not provide an adequate written description as to how the requisite sequencing is to be performed when the nucleotides are scanned at any power and from any angle.

8. Page 20 of the specification states, in part:

[0071] The problems are base discrimination at intersections and discrimination in the direction of depth. To solve these problems, the same sample is tilted at approximately 30° and another image is taken under this condition. In this way, depth information is obtained, and an image from which overlap has been removed is derived. Hence, two overlapping chemical elements can be discriminated. An analysis for performing this sequence of operations is the feature of the present system.

The claimed method, however, is not limited to tilting the sample at any angle, much less at an angle of 30 degrees, so to overcome problems associated with intersection and discrimination.

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While the specification asserts that it is possible to discriminate when two chemical elements overlap, the claimed method fairly encompasses sequencing complete chromosomes when there can be virtually any number of overlaps. The specification does not provide an adequate written description as to how such breadth of scope is to be obtained. In view of such immense breadth of scope encompassed by the claims and the limited description provided by the specification, the specification does not reasonably suggest that applicant was in possession of the invention at the time of filing. Accordingly, claims 1-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

9. Claims 1-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. As set forth in *Enzo Biochem Inc., v. Calgene, Inc.* (CAFC, 1999) 52 USPQ2d at 1135, bridging to 1136:

To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.' " *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)). Whether claims are sufficiently enabled by a disclosure in a specification is determined as of the date that the patent application was first filed, see *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986).... We have held that a patent specification complies with the statute even if a "reasonable" amount of routine experimentation is required in order to practice a claimed invention, but that such experimentation must not be "undue." See, e.g., *Wands*, 858 F.2d at 736-37, 8 USPQ2d at 1404 ("Enablement is not precluded by the necessity for some experimentation . . . However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' ") (footnotes, citations, and internal quotation marks omitted). In *In re Wands*, we set forth a number of factors which a court may consider in determining whether a disclosure would require undue experimentation. These factors were set forth as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of

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the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Id.* at 737, 8 USPQ2d at 1404. We have also noted that all of the factors need not be reviewed when determining whether a disclosure is enabling. See *Amgen, Inc. v. Chugai Pharm. Co., Ltd.*, 927 F.2d 1200, 1213, 18 USPQ2d 1016, 1027 (Fed. Cir. 1991) (noting that the *Wands* factors "are illustrative, not mandatory. What is relevant depends on the facts.").

10. It is well settled that one cannot enable an invention that they do not yet possess. As presented above, the specification does not reasonably suggest that applicant had possession of the invention at the time of filing. Therefore, the specification does not enable practicing the claimed invention. Accordingly, claims 1-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

11. Page 20 of the specification teaches in part:

[0070] The present analysis system is characterized in that it can analyze the sequence of single-chain DNA where the chain is bent and forms portions barely crossing each other, as well as a completely straight stretched a single-chain DNA. If the base spacing between chain portions close to an intersection is wide, bases can be discriminated based on the atomic number dependence intensity of the spot observed while tracing a single chain. Thus, the sequence can be determined. If no intersections are present, commercially available software can be used for analysis.

The claims, however, are not limited to sequencing but a single-chain DNA where it barely crosses its self, and is otherwise completely straight. The specification does not set forth a reproducible procedure whereby an overlapping chain can be sequences, even when purified from all other sequences. While the specification asserts that "commercially available software" can be sued, the specification does not identify suitable versions of said software, much less identify how they are to be modified such that they can be used to enable the claimed method. Rather than provide an enabling disclosure, the specification has been found to provide at best an

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invitation for others to experiment and ultimately determine how the claimed invention is to be practiced. Such an invitation to experiment does not constitute an enabling disclosure.

12. For the above reasons, and in the absence of convincing evidence to the contrary, claims 1-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

Conclusion

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571) 272-0751.

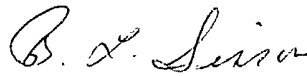
The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

14. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

15. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

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system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
15 November 2004